SUB C1 cont. 2. B1 cont

(Amended) A method for selectively inhibiting [proliferation of a] *transcription of NF-AT dependent genes in* hematopoietic cells [comprising

(i) causing the cell] engineered *ex vivo* to express an MBP gene encoding a mutated macrolide binding protein (MBP) [having an altered macrolide-binding specificity relative to a wild-type form of the MBP, which mutated MBP retains the ability to cause macrolide-dependent inhibition of proliferation; and

(ii)] which method comprises contacting the cells with a macrolide which selectively binds to the altered MBP relative to the wild-type MBP and [selectively] induces macrolide-dependent inhibition of [proliferation of cells expressing the mutated MBP relative to cells not expressing the wild-type MBP.] transcription of NF-AT dependent genes in the cells.

3. The method of claim 1 or 2, wherein the MBP is selected from the group consisting of a FRAP, an FK506-binding protein, a cyclophilin and a calcineurin.

4. **(Amended)** The method of claim 1 or 2, wherein the macrolide binds the mutated MBP with [has] a dissociation constant, Kd, at least one order of magnitude less than its [the] Kd for binding to [of the] wild-type MBP.

B2 5. **(Amended)** The method of claim 4, wherein the macrolide binds the mutated MBP with [has] a dissociation constant, Kd, at least three orders of magnitude less than its [the] Kd for binding to [of the] wild-type MBP.

SUB C2 6. **(Amended)** The method of claim 1 or 2, wherein the MBP gene was introduced into the cells by DNA transfection. [is present on an expression vector in the cell.]

C2 7. **(Amended)** The method of claim 1 or 2, wherein the MBP gene was introduced into the cells by virus-mediated transduction. [is present in the cell as part of a viral expression construct.]

8. **(Amended)** The method of claim 1 or 2, wherein the MBP gene was introduced into the cells by homologous recombination. [is a homologous recombinant in the cells genomic DNA.]

9. The method of claim 1 or 2, wherein the macrolide is an analog of rapamycin, FK506 or cyclosporin.

10. The method of claim 1 or 2, wherein the MBP gene encodes a FRAP protein, and the macrolide is an analog of rapamycin.

11. The method of claim 1 or 2, wherein the MBP gene encodes an FK506 binding protein, and the macrolide is an analog of FK506 or rapamycin.

12. The method of claim 1 or 2, wherein the MBP gene encodes a calcineurin protein, and the macrolide is an analog of FK506 or cyclosporin.

13. The method of claim 1 or 2, wherein the MBP gene encodes a cyclophilin protein, and the macrolide is an analog of cyclosporin.

14. The method of claim 1 or 2, wherein the cell is a mammalian cell.

15. The method of claim 1 or 2, wherein the cell is a human cell.

16. **(Amended)** A method for selectively inhibiting proliferation of a transplanted [hematopoietic] T cell comprising

(i) transplanting, into an animal, [hematopoietic] T cells which have been engineered to express an [a] MBP gene encoding a mutated macrolide binding protein (MBP), the mutated MBP having an altered macrolide-binding specificity relative to the wild-type form MBP

(ii) administering to the animal an amount of a macrolide sufficient to inhibit proliferation of the transplanted T cells, which macrolide selectively induces macrolide-dependent inhibition of proliferation of T cells expressing the mutated MBP compared to cells expressing a wild-type form of the MBP.

17. The method of claim 16, wherein the MBP is selected from the group consisting of a FRAP, an FK506-binding protein, a cyclophilin and a calcineurin.

18. **(Amended)** The method of claim 16, wherein the macrolide binds the mutated MBP with [has] a dissociation constant, Kd, at least one order of magnitude less than its [the] Kd for binding to [of the] wild-type MBP.

19. **(Amended)** The method of claim 16, wherein the macrolide binds the mutated MBP with [has] a dissociation constant, Kd, at least three orders of magnitude less than its [the] Kd for binding to [of the] wild-type MBP.

20. **(Amended)** The method of claim 16, wherein the MBP gene was introduced into the cells by DNA transfection. [is present on an expression vector in the cell.]

21. **(Amended)** The method of claim 16, wherein the MBP gene was introduced into the cells by virus-mediated transduction. [is present in the cell as part of a viral expression construct.]

22. **(Amended)** The method of claim 16, wherein the MBP gene was introduced into the cells by homologous recombination. [is a homologous recombinant in the cells genomic DNA.]

23. The method of claim 16, wherein the macrolide is an analog of rapamycin, FK506 or cyclosporin.

24. The method of claim 16, wherein the animal is a mammal.

25. The method of claim 24, wherein the animal is a human.

26. **(Amended)** The method of claim 16, wherein the transplanted T cells are autologous to the animal.

27. **(Amended)** The method of claim 16 or 26, wherein the transplanted T cells are present within [comprise] transplanted bone marrow.

28. **(Canceled)** The method of claim 16 or 26, wherein the transplanted cells comprise hematopoietic stem cells.

29. **(Amended)** The method of claim 16, wherein the [ectopic] expression of the mutated MBP gene is transcriptionally regulated by a T-cell specific transcriptional regulatory sequence.

30. The method of claim 16, wherein the animal is in an immunosuppressed state.

31. **(Amended)** A method for reducing graft-versus-host disease in an animal by selectively inhibiting proliferation of a transplanted [hematopoietic] T cell, comprising

(i) prior to transplanting [tissue containing a hematopoietic] the T cell, transducing [the [hematopoietic cell] it with a gene encoding [for ectopic expression of] a mutated macrolide binding protein (MBP), the mutated MBP having an altered macrolide-binding specificity relative to the wild-type form MBP; and

(ii) subsequent to transplanting the [hematopoeitic] T cell, administering to the animal an amount of a macrolide sufficient to inhibit proliferation of the [hematopoeitic] transplanted T cell, which macrolide selectively induces macrolide-dependent inhibition of proliferation of the transplanted T cell expressing the mutated MBP compared to endogenous cells of the animal, such that graft-versus-host disease is reduced.

32. **(Amended)** An expression construct encoding a mutated [macrolide binding protein (MBP) selected from the group consisting of] FRAP, FKBP, cyclophilin [and] or calcineurin, wherein the mutated [MBP] protein has an altered macrolide-binding specificity relative to [the] its wild-type form [MBP] and, in the presence of a macrolide to which it binds, [the mutated MBP,] induces macrolide-dependent inhibition of proliferation of a cell expressing the mutated [MBP] protein.

33. **(Amended)** A kit for [for] selectively inhibiting proliferation of a [hematopoietic] T cell, comprising

(i) an expression construct of claim 32 [for ectopically expressing an MBP gene encoding a mutated macrolide binding protein (MBP) having an altered macrolide-binding specificity relative to a wild-type form of the MBP, which mutated MBP retains the ability to cause macrolide-dependent inhibition of proliferation;] and

(ii) a macrolide which selectively binds to the altered protein [MBP] relative to the wild-type protein [MBP] and selectively induces macrolide-dependent inhibition of proliferation of T cells expressing the mutated MBP relative to T cells [not] expressing only the wild-type MBP.

34. **(Canceled)** A method of promoting engraftment and hematopoietic activity of a hematopoietic stem cell from a donor, comprising:

(a) inserting nucleic acid encoding a modified macrolide binding protein specific for a modified macrolide into a hematopoietic stem cell to produce a transformed hematopoietic stem cell;

(b) introducing the transformed hematopoietic stem cell into a recipient

mammal, such that the modified cellular receptor cyclophilin is expressed; and,

(c) administering an effective amount of the modified cyclosporin to said recipient mammal.

35. **(Canceled)** Hematopoietic stem cells transfected with the expression construct of claim 32.

36. A T cell transfected with an expression construct of claim 32.

37. **(Canceled)** A method for rendering a hematopoietic cell susceptible to inhibition by a modified macrolide, comprising transfecting isolated hematopoietic cells *ex vivo* with the construct of claim 32

38. **(Amended)** A method for rendering a [hematopoietic] T cell susceptible to inhibition by a [modified] macrolide, comprising transfecting [isolated hematopoietic] T cells *ex vivo* with a nucleic acid encoding [having a coding sequence for a polypeptide consisting essentially of a modified macrolide binding protein (] MBP [) having an altered macrolide-binding specificity relative to a wild-type form of the MBP,] to which the macrolide binds selectively relative to the unmodified MBP, which [mutated] modified MBP retains the ability to cause macrolide-dependent inhibition of proliferation of the T cell.

39. **(Amended)** The method of claim 38, comprising the further step of introducing the transfected [hematopoietic] T cell into a recipient mammal.

40. **(Canceled)** The method of claim 2, wherein the MBP gene has a coding sequence consisting essentially of a coding sequence for the mutated MBP.

41. **(Canceled)** The method of claim 3, wherein the MBP gene has a coding sequence consisting essentially of a coding sequence for the mutated MBP.

42. **(Canceled)** The method of claim 4, wherein the MBP gene has a coding sequence consisting essentially of a coding sequence for the mutated MBP.

43. **(Canceled)** The method of claim 9, wherein the MBP gene has a coding sequence consisting essentially of a coding sequence for the mutated MBP.